Mitochondrial DNA Variation and Disease Susceptibility in Primary Open-Angle Glaucoma

Singh LN (1) , Crowston JG (2) , Lopez Sanchez MIG (2) , Van Bergen NJ (2) , Kearns LS (2) , Hewitt AW (2,3) , Yazar S (4,5) , Mackey DA (4) , Wallace DC (1,6) , Trounce IA (2)

1 Center for Mitochondrial and Epigenomic Medicine, Children's Hospital of Philadelphia Research Institute, University of Pennsylvania, Philadelphia, United States.
2 Center for Eye Research Australia, Ophthalmology, University of Melbourne Department of Surgery, Melbourne, Australia.
3 Menzies Research Institute Tasmania, School of Medicine, University of Tasmania, Hobart, Australia.
4 Lions Eye Institute, University of Western Australia, Centre for Ophthalmology and Visual Science, Perth, Australia.
5 MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom.
6 Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, United States.

PURPOSE: To determine whether mitochondrial DNA haplogroups or rare variants associate with primary open-angle glaucoma in subjects of European descent.

METHODS: A case-control comparison of age- and sex-matched cohorts of 90 primary open-angle glaucoma patients and 95 population controls. Full mitochondrial DNA sequences from peripheral blood were generated by next-generation sequencing and compared to the revised Cambridge Reference Sequence to define mitochondrial haplogroups and variants.

RESULTS: Most subjects were of the major European haplogroups H, J, K, U, and T. Logistic regression analysis showed haplogroup U to be significantly underrepresented in male primary open-angle glaucoma subjects (odds ratio 0.25; 95% confidence interval http://CI 0.09-0.67; P = 0.007; Bonferroni multiple testing P = 0.022) . Variants in the mitochondrial DNA gene MT-ND2 were overrepresented in the control group (P = 0.005; Bonferroni multiple testing correction P = 0.015) .

CONCLUSIONS: Mitochondrial DNA ancestral lineages modulate the risk for primary open-angle glaucoma in populations of European descent. Haplogroup U and rare variants in the mitochondrial DNA-encoded MT-ND2 gene may be protective against primary open-angle glaucoma. Larger studies are warranted to explore haplogroup associations with disease risk in different ethnic groups and define biomarkers of primary open-angle glaucoma endophenotypes to target therapeutic strategies.

Invest Ophthalmol Vis Sci. 2018 Sep 4;59(11) :4598-4602. doi: 10.1167/iovs.18-25085.

30242360